# REMARKS

## I. Introduction

By the present Amendment, claims 1, 30, and 36 have been amended. No claims have been added or cancelled. Accordingly, claims 1-36 remain pending in the application. Claims 1 and 32 are independent.

## II. Office Action Summary

In the Office Action of September 28, 2007, the Disclosure was objected to because the Specification contained an embedded hyperlink. Claims 1-36 were rejected under 35 USC §112, second paragraph, as being indefinite. Claims 1-5, 9-12, 15-24, and 32-36 were rejected under 35 USC §102(b) as being anticipated by U.S. Patent No. 6,127,133 to Akong et al. ("Akong"). Claims 1 and 6-8 were rejected under 35 USC §103(a) as being unpatentable over Akong in view of U.S. Patent No. 5,532,128 issued to Eggers et al. ("Eggers"). Claims 1, 13, and 14 were rejected under 35 USC §103(a) as being unpatentable over Akong in view of Eggers, and further in view of U.S. Patent No. 6,448,983 to Ali et al. ("Ali"). Claims 1 and 25-29 were rejected under 35 USC §103(a) as being unpatentable over Akong in view of Eggers, and further in view of U.S. Patent No. 5,808,918 issued to Fink et al. ("Fink"). Claims 1, 30, and 31 were rejected under 35 USC §103(a) as being unpatentable over Akong in view of Eggers, and further in view of Terramani et al. ("Terramani"). These rejections are respectfully traversed.

## III. Objection to the Disclosure

The Disclosure was objected to because the Specification contained an embedded hyperlink. The Office Action further indicated that the embedded link should be removed pursuant to MPEP §608.01.

By the present Amendment, Applicants have amended the Specification to remove the embedded hyperlink. Withdrawal of this rejection is therefore respectfully requested.

## IV. Rejections under 35 USC §112

Claims 1-36 were rejected under 35 USC §112, as being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. Regarding this rejection, the Office Action alleges that claims 1 and 32 recite the limitation of "mapping or maps." The Office Action indicates that it is unclear how these terms should be interpreted.

Applicants respectfully disagree with this rejection, and request reconsideration in view of the following. As can be appreciated, the present invention relates to a computer-implemented screening method which utilizes, in part, statistical and analytical processing. In this regard, any type of mapping performed by the software program, or computer system, would necessarily relate to computer programming and/or data management. Within this field, it is well known to those skilled in the art that mapping of one value, or object, to another corresponds to the establishment of a relationship between the two. Clearly, as used in claims 1 and 32, the term mapping is intended to define a relationship that is established between the two items and/or a representation of one item by the other.

Applicants respectfully submit that claims 1 and 32 are not indefinite because the term "mapping" would be clearly understood by one of ordinary skill in the art. Withdrawal of this objection is therefore respectfully requested.

The Office Action further indicated that claim 1 recited the limitation "and/or or," and that this alternative combination of limitations was unclear.

By the present Amendment, Applicants have amended independent claim 1, to correct this error and resolve the issues raised in the Office Action. Withdrawal of this objection is therefore respectfully requested.

## V. Rejections under 35 USC §102

Claims 1-5, 9-12, 15-24, and 32-36 were rejected under 35 USC §102(b) as being anticipated by Akong. Regarding this rejection, the Office Action alleges that Akong discloses an automated method of identifying agents such as growth effector molecules, that cause a phenotypic change in a cell, such as a desired biological response. The Office Action asserts that Akong discloses the addition of drug compounds that effect the muscarinic and nicotinec receptors and calcium ions of various cell lines by using a software program that generates a computer representation of a statistical design that includes generic factor names, factor levels and experimental runs on an array of wells. The Office Action further asserts that Akong discloses contacting the cells with drug compounds, utilizing a microprocessor with equations to compare the fluorescence data and statistical design to determine the effective drugs that effect muscarinic and acetylcholine receptors, nicotine acetylcholine receptors and calcium channels, and storing this statistical design and drug data in tables and on disk. Applicants respectfully disagree.

According to the present invention, as defined by independent claim 1, an automated method is provided for identifying agents that cause a phenotypic change in a cell. The method comprises the steps of:

> providing receptacles in an array;
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> providing a statistical design including generic factor names, factor levels, and experimental runs;
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> utilizing a software program to generate a computer representation of said statistical design, said computer representation being generated by automatically mapping the identities of agents to said generic factor names, by mapping the concentration or amounts of said agents to said factor levels, and by mapping the locations of said receptacles within said array to said experimental runs;
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> placing different mixtures of single said agents into select ones of said receptacles in said array according to said computer representation of said statistical design;
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> contacting said placed mixtures with said cells;
>
> acquiring data indicative of a phenotypic change in said contacted cells;
>
> utilizing a processor including an algorithm for comparing said phenotypic data with said statistical design to identify which of said mixtures of single agents and/or which of said single agents in said mixtures are effective in causing said phenotypic change in said contacted cells; and
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> storing said statistical design, said agent identities, said computer representation of said statistical design, said acquired data, and the results of said algorithm comparison in one or more databases.

The automated method of independent claim 1 provides a number of receptacles and an array, as well as a statistical design that includes generic factor names, factor levels, and experimental runs. A software program is utilized to generate a computer representation of the statistical design by automatically mapping the identities of agents to the generic factor names, mapping the concentration or amounts of the agents to the factor levels, and mapping the locations of the receptacles within the array to the experimental runs. Different

mixtures of single agents are placed into select receptacles in the array according to the computer representation of the statistical design. The mixtures are contacted with the cells, and data indicative of a phenotypic change of the contacted cells is acquired. A processor, including an algorithm for comparing the phenotypic data with the statistical design, is utilized to identify which of the mixtures of the single agents or which of the single agents in the mixtures are effective in causing the phenotypic change in the contacted cells. The statistical design, agent identities, computer representation of the statistical design, acquired data, and results of the algorithm comparison are subsequently stored in one or more databases.

The Office Action alleges that Akong discloses all the features of the claimed invention and cites various passages where these features are supposedly disclosed. Applicants' review of Akong, however, has revealed various differences from the claimed invention. At the outset, Applicants note that Akong discloses an automated analysis equipment and assay method. The apparatus of Akong is intended to automate the process of adding a single reagent to samples and measuring the reaction results in order to minimize lab worker time requirements. As shown in Fig. 5, the device uses a syringe/plunger (135/137) arrangement to draw and pump the reagent from a reagent vessel (145). See col. 6, ln. 58 – col. 7, ln. 4. Accordingly, Akong only automates the process of supplying the same reagent into the assay system. Consequently, it is not possible to place different mixtures of agents (or reagents) into selected receptacles, as set forth in the claimed invention.

The Office Action indicates that Akong discloses a statistical design. The cited passages, however, appear to relate only to the X,Y locations of each specific well within the rectangular array. See col. 5, ln. 15 – 30. There is no discussion of a statistical design involving, for example, the mapping of different agents. This is to

be expected, as Akong utilizes the same agent in all the wells. Akong further discloses that "a test consists of the assay of one or more wells using substantially the same test parameter values," further supporting the use of the same agent. See col. 7, ln. 49 – 51. Likewise, the remaining passages cited in the Office Action only relate to examples wherein the same reagent is used in all the wells. Akong also discloses a data file which keeps track of the compound/concentration in each well. See Fig. 6 and 7, and corresponding passage. Although various equations are disclosed, they are only useable for calculating the fluorescence signal-to-noise ratio and intracellular signal-to-noise ratio. See col. 19, ln. 1 – 30. This is clearly not intended to represent a statistical design as set forth in the claimed invention.

Contrary to the assertions made in the Office Action, Akong does not disclose identification of agents that cause a phenotypic change. As previously discussed, only one reagent is used in all the wells during the screening process. Akong discloses an automated assay process wherein the phenotype does not change. The process only measures the phenotype of the cells by determining how they react to one specific agent. See col. 2, ln. 53 – 57. Additionally, Akong merely discusses contacting the cells with a compound. There is no discussion of culturing the cells with multiple, or even one, compounds. Regardless of the manner in which the cells are contacted, however, it is not possible for Akong to obtain data indicative of phenotypic change because the phenotype in Akong's assays does not change.

Furthermore, Akong does not discuss storing the statistical design in a database. Only the data from cells treated in the same manner are collected and recorded. As previously discussed, Akong does not create a statistical design. Consequently, it is unclear how a statistical design, in part, could be stored in one or more databases. As can be appreciated, a database is vastly different from a simple

data file which can easily be represented by a one or two-dimensional array. A database provides relationships between different tables and entries, and can be queried by users to filter and retrieve various information. Merely storing data into a file is certainly not the same as storing (and interrelating) information in a database.

In contrast, the present invention provides an iterative process that actually solves a problem as opposed to simply collecting test data. See paragraphs [0035] and [0036]. This can be achieved, for example, by utilizing different agents and/or mixtures of agents and exploring interactions between mixtures of different factors in order to achieve a desired cell fate. Rather than simply measuring the phenotype of the cell, the method of independent claim 1 actually attempts to change the phenotype. See paragraph [0004] of the published application. Akong simply fails to provide any disclosure or suggestion for features recited in independent claim 1 such as:

> providing a statistical design including generic factor names, factor levels, and experimental runs;
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> utilizing a software program to generate a computer representation of said statistical design, said computer representation being generated by automatically mapping the identities of agents to said generic factor names, by mapping the concentration or amounts of said agents to said factor levels, and by mapping the locations of said receptacles within said array to said experimental runs;
>
> placing different mixtures of single said agents into select ones of said receptacles in said array according to said computer representation of said statistical design;
>
> contacting said placed mixtures with said cells;
>
> acquiring data indicative of a phenotypic change in said contacted cells;
>
> utilizing a processor including an algorithm for comparing said phenotypic data with said statistical design to identify which of said mixtures of single agents and/or which of said single agents in said mixtures are effective in causing said phenotypic change in said contacted cells; and

storing said statistical design, said agent identities, said computer representation of said statistical design, said acquired data, and the results of said algorithm comparison in one or more databases.

It is therefore respectfully submitted that independent claim 1 is allowable over the art of record.

Claims 2 – 31 depend from independent claim 1, and are therefore believed allowable for at least the reasons set forth above with respect to independent claim 1. In addition, these claims each introduce novel elements that independently render them patentable over the art of record.

Independent claim 32 defines a system for identifying agents that cause a phenotypic change in a cell. The system comprises:

an array of receptacles, selective ones of which are for receiving (i) different mixtures of single said agents, and (ii) fluid including said cells;

a statistical design including generic factor names, factor levels, and experimental runs;

a software program for generating a computer representation of said statistical design, wherein said software program automatically maps the identities of said agents to said generic factor names, maps the concentration of or amounts of said agents to said factor levels, and maps the locations of said receptacles in said array to said experimental runs;

acquired experimental data indicative of said phenotypic change in said cells;

a processor including an algorithm for comparing said experimental data with said statistical design to identify which of said mixtures of single agents and/or which of said single agents in said mixtures are effective in causing said phenotypic change in said cells; and

one or more databases for storing said statistical design, said agent identities, said computer representation of said statistical design, said acquired experimental data, and the results of said algorithm comparison.

According to the system of independent claim 32, an array of receptacles is provided to receive different mixtures of agents and fluids that include cells. A statistical design is provided to include generic factor names, factor levels, and experimental runs. A software program generates a computer representation of the statistical design, in part, by mapping the identities of the agents to the generic factor names, mapping the concentration or amounts of the agents to the factor levels, and mapping the locations of the receptacles in the array to the experimental runs. The system also includes a processor including an algorithm for comparing acquired experimental data indicative of phenotypic change in the cells with the statistical design. The processor further identifies which of the agents in the mixtures are effective in causing the phenotypic change in the cells. One or more databases are also provided for storing the statistical design, the acquired experimental data, and the result of the algorithm comparison.

The elements recited in the system of independent claim 32 are configured to perform functions that are somewhat similar to the steps recited in independent claim 1. As previously discussed, Akong fails to provide any disclosure or suggestion for various features of the claimed invention. For example, Akong fails to disclose the use of multiple agents or the creation of a statistical design. In fact, Akong only discloses the use of a single reagent and measurement of results which do not involve a change in the phenotype. Consequently, there can be no disclosure or suggestion for acquiring data indicative of a phenotypic change, or a comparison of the phenotypic data with the statistical design to determine which agent(s) are effective in causing the phenotypic change in the cells.

It is therefore respectfully submitted that independent claim 32 is allowable over the art of record.

Claims 33 – 36 depend from independent claim 32, and are therefore believed allowable for at least the reasons set forth above with respect to independent claim 32. In addition, these claims each introduce novel elements that independently render them patentable over the art of record.

## VI. Rejections under 35 USC §103

Claims 1 and 6-8 were rejected under 35 USC §103(a) as being unpatentable over Akong in view of Eggers. Claims 1, 13, and 14 were rejected under 35 USC §103(a) as being unpatentable over Akong in view of Eggers, and further in view of Ali. Claims 1 and 25-29 were rejected under 35 USC §103(a) as being unpatentable over Akong in view of Eggers, and further in view of Fink. Claims 1, 30, and 31 were rejected under 35 USC §103(a) as being unpatentable over Akong in view of Eggers, and further in view of Terramani.

At the outset, Applicants note that claim 1 has now been rejected under 35 USC §103(a) as being unpatentable over a combination of references. In rejecting these claims, the Office Action relies on the secondary and tertiary references to disclose the features not shown in Akong. It thus appears that the Office Action is admitting that Akong fails to disclose at least some of the features recited in independent claim 1. Consequently, the rejection predicated on 35 USC §102(b) would appear to be improper because all the features recited in independent claim 1 are now indicated as not being disclosed by the primary reference (Akong) under 35 USC §103(a).

Furthermore, as previously discussed with respect to independent claim 1, Akong fails to disclose numerous features recited in this claim. Applicants' review of the references applied in combination with Akong, has also failed to reveal any

disclosure or suggestion for the same features that are lacking in Akong. Consequently, any combination of these references necessarily fails to disclose or suggest all of the features recited in independent claim 1.

It is therefore respectfully submitted that independent claim 1 is allowable over the combination of applied references.

Claims 6 – 8, 13, 14, and 25 – 31 depend from independent claim 1, and are therefore believed allowable for at least the reasons set forth above with respect to independent claim 1.

## VII. Conclusion

For the reasons stated above, it is respectfully submitted that all of the pending claims are now in condition for allowance. Therefore, the issuance of a Notice of Allowance is believed in order, and courteously solicited.

If the Examiner believes that there are any matters which can be resolved by way of either a personal or telephone interview, the Examiner is invited to contact Applicants' undersigned attorney at the number indicated below.

## AUTHORIZATION

It is respectfully requested that any shortage in the fee be charged to the account of Becton, Dickinson and Company (ATSK), Account No. 06-4154 (Case No. P-5768(1385.45509X00)).

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Respectfully submitted,
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